Hypoxia selectively inhibits KCNA5 channels in pulmonary artery smooth muscle cells.

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Public Summary:

Scientific Abstract:
Acute hypoxia induces pulmonary vasoconstriction and chronic hypoxia causes pulmonary vascular remodeling characterized by significant vascular medial hypertrophy. Electromechanical and pharmacomechanical mechanisms are involved in regulating pulmonary vasomotor tone, while changes in cytosolic Ca2+ concentration ([Ca2+](cyt)) are an important signal in regulating contraction and proliferation of pulmonary artery smooth muscle cells (PASMC). Hypoxia-induced increases in [Ca2+](cyt) are, in part, mediated by selective inhibition of voltage-gated K+ (Kv) channels in PASMC. Kv1.5, encoded by the KCNA5 gene, is a Kv channel alpha subunit that forms functional homotetrameric and heterotetrameric Kv channels in PASMC. Activity of Kv channels contributes to the regulation of resting membrane potential. Overexpression of the human KCNA5 gene in rat PASMC and other cell types increases whole-cell Kv currents and causes membrane hyperpolarization. However, acute hypoxia only reduced Kv currents in KCNA5-transfected PASMC. These results provide compelling evidence that Kv1.5 is an important hypoxia-sensitive Kv channel in PASMC, contributing to regulation of membrane potential and intracellular Ca2+ homeostasis during hypoxia. This hypoxia-sensitive mechanism essential for inhibiting Kv1.5 channel activity is exclusively present in PASMC.